REMARKS

I. Status of the Claims

Claims 1-88 were originally filed and later canceled. Claims 89-124 were subsequently added. Claims 93, 97-103, and 107-130 are currently pending under examination.

Claims 93 and 103 are amended to recite that the HER-2/Neu fusion protein does not comprise any portion of a HER-2/Neu transmembrane domain, which is supported by the specification, *e.g.*, on page 7, lines 18-25. Claims 93 and 103 are further amended to recite the fusion protein is capable of inducing an immunity against a HER-2/Neu protein in a warm-blooded animal, which finds support in the specification, *e.g.*, on page 6, lines 26-30.

The present amendment introduces no new matter and requires no new searches. Its entry is respectfully requested.

II. Claim Rejections

A. 35 U.S.C. §112, First Paragraph: Written Description

Claims 93, 97-103, 107-116, 121, and 124-130 remained rejected under 35 U.S.C. §112, first paragraph, for alleged failure to meet the written description requirement. The Examiner asserted two reasons for this rejection: first, the genus of nucleic acids encoding the claimed fusion proteins, which, following the amendment filed by Applicants on March 5, 2004, are defined by the at least 90% sequence identity to SEQ ID NO:6 or SEQ ID NO:7, finds no support in the specification; second, the genus of nucleic acids encoding HER-2/Neu fusion proteins is not adequately described, because the exemplary structures provided are not representative of the claimed genus (last paragraph on page 2 of the Final Office Action). Applicants respectfully traverse the rejection, particularly in light of the present amendment.

Basis for Claim Amendment

The Examiner first alleged that Applicants' claim amendment filed March 5, 2004, which amends claims 93 and 103 to recite a HER-2/Neu fusion protein "at least 90% identical to" SEQ ID NO:6 or SEQ ID NO:7, is not properly supported by the specification. Applicants respectfully disagree with the Examiner on this point.

By reciting the at least 90% sequence identity, Applicants are defining the claimed genus of nucleic acids encoding HER-2/Neu fusion proteins based on the fusion proteins' similarity in amino acid sequence in relation to a reference sequence, SEQ ID NO:6 or SEQ ID NO:7. The similarity or identity between two amino acid or polynucleotide sequences is described in the specification, *e.g.*, on page 9, lines 27-32, and page 10, lines 4-6, where it is stated that "[m]ore preferred embodiments include at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% [to a reference sequence]." Therefore, even though the two sequence identifiers are not expressly named in this paragraph, a sequence identity of any of the above-mentioned percentages to SEQ ID NO:6 or SEQ ID NO:7 is fully supported.

Written Description for the Claimed Genus

The Examiner also alleged that the specification does not provide sufficient written description for the claimed genus of nucleic acids. Applicants again respectfully disagree with the Examiner.

According to the MPEP, to satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. Possession of a claimed invention may be demonstrated by description of the

invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. MPEP §2163 I.

Case law indicates that structural features of a claimed invention can be essential to satisfy the written description requirement. The Federal Circuit in *Fiers v. Revel*, 25 USPQ2d 1601 (Fed. Cir. 1993), stated that an adequate written description "requires a precise definition, such as by structure, formula, chemical name, or physical properties." *Fiers*, 25 USPQ2d at 1606. The requirement for written description of a chemical genus is further set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). As described by the Federal Circuit in *Lilly*, "[a] description of a genus of cDNAs may be achieved by means of . . . a recitation of structural features common to the members of the genus . . . ." *Lilly*, 43 USPQ2d at 1406.

On the other hand, proper description of functional features of a claimed invention can also play an important role in satisfying the written description requirement. The Federal Circuit recently stated that "*Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 65 USPQ2d 1385, 1398 (Fed. Cir. 2003).

As amended, pending claims are directed to a nucleic acid encoding a HER-2/Neu fusion protein, which: (1) consists of a HER-2/Neu ECD and a HER-2/Neu Pd (or ΔPD), (2) does not comprise any portion of a HER-2/Neu transmembrane domain,

(3) is at least 90% identical to SEQ ID NO:6 (or SEQ ID NO:7), and (4) is capable of producing an immune response against a HER-2/Neu protein in a warm-blooded animal. Applicants contend that the pending claims fully comply with the requirements for written description of a chemical genus as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). With regard to the claimed nucleic acids, claims 93 and 103 (and their dependent claims) set forth both functional elements, *e.g.*, encoding fusion proteins capable of producing an immune response against a HER-2/Neu protein in a warm-blooded animal, as well as structural elements, *e.g.*, encoding fusion proteins having a certain percentage sequence identity to a reference amino acid sequence. Applicants submit, therefore, that the claimed nucleic acids are thereby defined via shared functional and structural properties.

The amino acid sequence of a polypeptide, such as a HER-2/Neu fusion protein, is a physical/structural property of the molecule. Thus, it is also a physical/structural property of a polypeptide to have a certain percentage sequence identity to a reference amino acid sequence, because such percentage identity relies entirely upon the primary amino acid sequence of the polypeptide. Moreover, because the amino acid sequence of a polypeptide is determined by the polynucleotide sequence encoding this polypeptide, such amino acid sequence identity is also a physical/structural property of a nucleic acid encoding the polypeptide.

The functional features of the claimed nucleic acids are also provided by the description of the functions of the HER-2/Neu fusion proteins encoded by the nucleic acids: each of the fusion protein is capable of inducing an immunity against a HER-2/Neu

protein in a warm-blooded animal. As required by the standard set forth in *University of California v. Eli Lilly,* these features are common to all members of the claimed genus.

Thus, both structural and functional features commonly shared by the claimed genus have been described in detail, which "clearly allow persons of ordinary skill in the art to recognize that [the applicant] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991).

The Examiner in addition raised the concern that the claimed genus of nucleic acids may encompass those encoding polypeptides that comprise a domain highly similar to one HER-2/Neu domain (*i.e.*, one of ECD, PD, and ΔPD) fused to only a few amino acids from a second HER-2/Neu domain. Applicants contend that the nucleic acid encoding such a fusion protein would not be within the scope of the currently pending claims. Since a HER-2/Neu fusion protein as defined by currently pending claims has to maintain an amino acid sequence identity no less than 90% to SEQ ID NO:6 (fusion of human ECD and human PD) or SEQ ID NO:7 (fusion of human ECD and human ΔPD), it is impossible for such a protein to include only a small portion of either ECD, PD, or ΔPD.

In summary, the claimed genus of nucleic acids encoding HER-2/Neu fusion proteins is described by a recitation of structural and functional features common to the members of the genus. The pending claims fully comply with the written description requirement as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) and *Fiers v. Revel*, 25 USPQ2d 1601 (Fed. Cir. 1997), and "clearly allow persons of ordinary skill in the art to recognize that [the applicant]

invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). The withdrawal of written description rejection is respectfully requested.

B. 35 U.S.C. §102

1. Kipps et al.

Claims 93, 97-103, 107-112, 117, 118, and 122 remained rejected under 35 U.S.C. §102(e) for alleged anticipation by Kipps *et al.* (U.S. Patent No. 6,287,569). Applicants respectfully traverse the rejection in light of the present amendment.

To anticipate a pending claim, a prior art reference must provide all limitations of the claim. MPEP §2131. As amended, independent claims 93 and 103 are drawn to an isolated nucleic acid encoding a polypeptide comprising a HER-2/Neu fusion protein, which consists of a HER-2/Neu extracellular domain (ECD) linked to a HER-2/Neu phosphorylation domain (PD) or a fragment of PD (ΔPD) and does not comprise any portion of a HER-2/Neu transmembrane domain, has at least 90% identity to SEQ ID NO:6 or SEQ ID NO:7, and is capable of producing an immune response against a HER-2/Neu protein in a warm-blooded animal.

In contrast, Kipps *et al.* disclose a nucleic acid encoding a chimeric immunogen that comprises a full length HER-2/Neu protein. The limitation of a HER-2/Neu fusion protein not comprising any portion of a HER-2/Neu transmembrane domain is not present in the Kipps *et al.* reference. Therefore, claims 93 and 103, as well as their dependent claims, are not anticipated by Kipps *et al.* Accordingly, the anticipation rejection should be properly withdrawn.

2. Hudziak et al.

Claims 93, 97, 102, 103, 107, 112, 113, 117, and 118 remained rejected under 35 U.S.C. §102(e) for alleged anticipation by Hudziak *et al.* (U.S. Patent No. 6,015,567). Applicants respectfully traverse the rejection in light of the present amendment.

As discussed above, to anticipate a pending claim, all claim limitations must be present in a prior art reference. The Hudziak *et al.* reference discloses a mutated Her-2/Neu protein, $p185^{HER2\Delta TM}$, that has 28 amino acids in its transmembrane domain deleted (Fig. 1B and description in column 3, lines 9-11). This disclosure does not describe a HER-2/Neu fusion protein not comprising any portion of a Her-2/Neu transmembrane domain. As such, the Hudziak reference does not anticipate the pending claims. The withdrawal of the anticipation rejection on this ground is respectfully requested.

C. 35 U.S.C. §103

1. Kipps et al. in View of Carrano et al.

Claims 93, 99-101, 103, 109-111, and 125-129 remained rejected under 35 U.S.C. §103(a) for alleged obviousness over Kipps *et al.* in view of Carrano *et al.* (U.S. Patent No. 5,962,428). Applicants respectfully traverse the rejection in light of the present amendment.

To establish a *prima facie* case of obviousness, three basic criteria must be met: first, the prior art references must teach or suggest all the claim limitations; second, there must be some suggestion or motivation, either in the references or in the knowledge generally available to one of ordinary skill in the art, to combine the limitations; third, there must be a reasonable expectation of success in combining the limitations. MPEP §2143.

As discussed above, the Kipps *et al.* reference does not provide all limitations of independent claims 93 and 103. The Carrano *et al.* reference is cited for the purpose of providing the limitation of immunostimulatory substances and does not complement the Kipps *et al.* reference in providing all limitations of claims 93 and 103. As such, the Kipps and Carrano references together fail to provide all limitations of the pending claims. No *prima facie* case of obviousness has been established. Applicants

thus respectfully request that the Examiner withdraw the obviousness rejection based on these two references.

2. Kipps et al. in View of Krieg et al.

Claims 93, 99-101, 103, 109-111, and 130 remained rejected under 35 U.S.C. §103(a) for alleged obviousness over Kipps *et al.* in view of Krieg *et al.* (U.S. Patent No. 6,429,199). Applicants traverse the rejection in light of the present amendment.

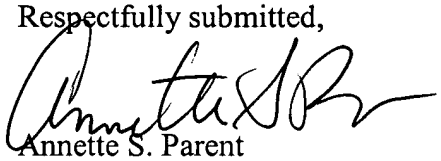
As discussed in the last section, the Kipps *et al.* reference does not provide all limitations of the pending claims. The Krieg *et al.* reference merely provides the limitation of using CpG oligonucleotides in vaccine compositions and does not supplement the missing limitation of a HER-2/Neu fusion protein consisting of an ECD and a PD (or ΔPD). The two cited references therefore do not combinedly provide all limitations of the pending claims. No *prima facie* obviousness has been established. Accordingly, Applicants respectfully submit that the obviousness rejection based on the Kipps and Krieg references is improper and should be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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